



## Complete Summary

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### GUIDELINE TITLE

Surviving sepsis campaign guidelines for management of severe sepsis and septic shock.

### BIBLIOGRAPHIC SOURCE(S)

Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, Ramsay G, Zimmerman JL, Vincent JL, Levy MM. Surviving sepsis campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004 Mar; 32(3):858-73. [135 references] [PubMed](#)

## COMPLETE SUMMARY CONTENT

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

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## SCOPE

### DISEASE/CONDITION(S)

- Severe sepsis
- Septic shock

### GUIDELINE CATEGORY

Management  
Treatment

### CLINICAL SPECIALTY

Critical Care  
Emergency Medicine  
Internal Medicine  
Nursing  
Pediatrics

## INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Hospitals  
Nurses  
Physician Assistants  
Physicians

## GUIDELINE OBJECTIVE(S)

- To present practical guidelines for the bedside clinician on the management of patients with severe sepsis and septic shock
- To increase international awareness and improve outcomes in severe sepsis

## TARGET POPULATION

Adult and pediatric patients in intensive care unit (ICU) settings (and sometimes in the pre-ICU settings) with severe sepsis and septic shock

## INTERVENTIONS AND PRACTICES CONSIDERED

1. Initial resuscitation
2. Diagnostic studies, as indicated
  - Blood cultures and cultures from other sites, as indicated, such as urine, cerebrospinal fluid, wounds, respiratory secretions, or other body fluids
  - Imaging studies, as indicated, such as ultrasound
3. Antibiotic therapy
4. Source control measures
5. Fluid therapy
  - Natural or artificial colloids or crystalloids
  - Fluid challenge in patients with suspected hypovolemia
6. Vasopressor therapy as needed (norepinephrine, dopamine, vasopressin)
7. Inotropic therapy (dobutamine or a combination of dobutamine and a vasopressor) as indicated
8. Steroids (hydrocortisone with or without fludrocortisone, dexamethasone)
9. Recombinant human activated protein C (rhAPC)
10. Blood product administration (red blood cell transfusion, erythropoietin, fresh frozen plasma, antithrombin\*, platelets)
11. Mechanical ventilation of sepsis-induced acute lung injury (ALI)/adult respiratory distress syndrome (ARDS)
12. Sedation, analgesia, and neuromuscular blockade
13. Glucose control
14. Renal replacement (hemofiltration, hemodialysis)
15. Bicarbonate therapy\*
16. Deep vein thrombosis (DVT) prophylaxis (low-dose unfractionated heparin, low-molecular weight heparin, mechanical prophylactic devices)
17. Stress ulcer prophylaxis (H2 receptor inhibitors)
18. Consideration for limitation of support
19. Pediatric considerations

\*Guideline developers considered but did not recommend these measures.

## MAJOR OUTCOMES CONSIDERED

- Survival of patients with severe sepsis and septic shock
- Length of stay in the intensive care unit (ICU)

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The 2001 publication that was used as a starting point for the current process included a MEDLINE search for clinical trials in the preceding 10 years, supplemented by a manual search of other relevant journals. Subtopics for each recommendation were cross-referenced to sepsis, severe sepsis, septic shock, sepsis syndrome, and infection. The Surviving Sepsis Campaign guidelines considered the evidence in the 2001 publication (through 1999) and repeated the process for 2000 through 2003.

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grading of Evidence

- I. Large, randomized trials with clear-cut results; low risk of false-positive (alpha) error or false-negative (beta) error
- II. Small, randomized trials with uncertain results; moderate-to-high risk of false-positive (alpha) and/or false-negative (beta) error
- III. Nonrandomized, contemporaneous controls
- IV. Nonrandomized, historical controls and expert opinion
- V. Case series, uncontrolled studies, and expert opinion

### METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Each clinical trial used to support recommendations was graded based on the methodology in Table 1 of the original guideline document and included presence or absence of important elements such as concealed randomization, blinded outcome adjudication, intention to treat analysis, and explicit definition of primary outcome. All articles were initially reviewed based on subgroup assignments and typically by two or three participants. Survival (28–30 days) was the standard outcome measure used to assess outcome benefit, and when an alternative was used, this is stated in the rationale (see the original guideline document). Where strong trial evidence existed for outcome benefit in critically ill populations known to contain a larger number of sepsis patients, these trials were considered in determination of recommendation grading.

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)  
Expert Consensus (Delphi)

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The guideline development process included a modified Delphi method, a consensus conference, several subsequent smaller meetings of subgroups and key individuals, teleconferences, and electronic-based discussion among subgroups and among the entire committee.

The goal was total consensus, which was reached in all recommendations except two. In those circumstances (recommendations C3 and H1), the solution was achieved with the inclusion of subrecommendations that expressed some difference in expert opinion. When there was difference of opinion about grading of a clinical trial, an outside epidemiologist was consulted. This occurred in one circumstance with resolution of differences.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

### Grading of Recommendations

- A. Supported by at least two level I investigations
- B. Supported by one level I investigation
- C. Supported by level II investigations only
- D. Supported by at least one level III investigation
- E. Supported by level IV or V evidence

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The document was finalized and approved by the consensus committee and by sponsoring organizations in December 2003.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The grades of recommendations (A-E) and grades of evidence (I-V) are defined at the end of the "Major Recommendations" field.

#### A. Initial Resuscitation

1. The resuscitation of a patient in severe sepsis or sepsis-induced tissue hypoperfusion (hypotension or lactic acidosis) should begin as soon as the syndrome is recognized and should not be delayed pending intensive care unit (ICU) admission. An elevated serum lactate concentration identifies tissue hypoperfusion in patients at risk who are not hypotensive. During the first 6 hrs of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as one part of a treatment protocol:
  - Central venous pressure: 8–12 mm Hg
  - Mean arterial pressure  $\geq 65$  mm Hg
  - Urine output  $\geq 0.5$  mL/kg/hr
  - Central venous (superior vena cava) or mixed venous oxygen saturation  $\geq 70\%$

Grade of Recommendation B

2. During the first 6 hrs of resuscitation of severe sepsis or septic shock, if central venous oxygen saturation or mixed venous oxygen saturation of 70% is not achieved with fluid resuscitation to a central venous pressure of 8–12 mm Hg, then transfuse packed red blood cells to achieve a hematocrit of  $\geq 30\%$  and/or administer a dobutamine infusion (up to a maximum of 20 micrograms/kg/min) to achieve this goal.

Grade of Recommendation: B

#### B. Diagnosis

1. Appropriate cultures should always be obtained before antimicrobial therapy is initiated. To optimize identification of causative organisms, at least two blood cultures should be obtained with at least one drawn percutaneously and one drawn through each vascular access device, unless the device was recently (<48 hrs) inserted. Cultures of other sites such as urine, cerebrospinal fluid, wounds, respiratory secretions, or other body fluids should be obtained before antibiotic therapy is initiated as the clinical situation dictates.

Grade of Recommendation: D

2. Diagnostic studies should be performed promptly to determine the source of the infection and the causative organism. Imaging studies and sampling of likely sources of infection should be performed; however, some patients may be too unstable to warrant certain invasive procedures or transport outside of the ICU. Bedside studies, such as ultrasound, may be useful in these circumstances.

Grade of Recommendation: E

#### C. Antibiotic Therapy

1. Intravenous antibiotic therapy should be started within the first hour of recognition of severe sepsis, after appropriate cultures have been obtained.

Grade of Recommendation: E

2. Initial empirical anti-infective therapy should include one or more drugs that have activity against the likely pathogens (bacterial or fungal) and that penetrate into the presumed source of sepsis. The choice of drugs should be guided by the susceptibility patterns of microorganisms in the community and in the hospital.

Grade of Recommendation: D

3. The antimicrobial regimen should always be reassessed after 48–72 hrs on the basis of microbiological and clinical data with the aim of using a narrow-spectrum antibiotic to prevent the development of resistance, to reduce toxicity, and to reduce costs. Once a causative pathogen is identified, there is no evidence that combination therapy is more effective than monotherapy. The duration of therapy should typically be 7–10 days and guided by clinical response.

Grade of Recommendation: E

- a. Some experts prefer combination therapy for patients with *Pseudomonas* infections.

Grade of Recommendation: E

- b. Most experts would use combination therapy for neutropenic patients with severe sepsis or septic shock. For neutropenic patients, broad-spectrum therapy usually must be continued for the duration of the neutropenia.

Grade of Recommendation: E

4. If the presenting clinical syndrome is determined to be due to a noninfectious cause, antimicrobial therapy should be stopped promptly

to minimize the development of resistant pathogens and superinfection with other pathogenic organisms.

Grade of Recommendation: E

#### D. Source Control

1. Every patient presenting with severe sepsis should be evaluated for the presence of a focus on infection amenable to source control measures, specifically the drainage of an abscess or local focus on infection, the debridement of infected necrotic tissue, the removal of a potentially infected device, or the definitive control of a source of ongoing microbial contamination. (See Appendix A in the original guideline document for examples of potential sites needing source control.)

Grade of Recommendation: E

2. The selection of optimal source control methods must weigh benefits and risks of the specific intervention. Source control interventions may cause further complications such as bleeding, fistulas, or inadvertent organ injury; in general, the intervention that accomplishes the source control objective with the least physiologic upset should be employed, for example, consideration of percutaneous rather than surgical drainage of an abscess.

Grade of Recommendation: E

3. When a focus of infection amenable to source control measures, such as an intra-abdominal abscess, a gastrointestinal perforation, cholangitis, or intestinal ischemia, has been identified as the cause of severe sepsis or septic shock, source control measures should be instituted as soon as possible following initial resuscitation.

Grade of Recommendation: E

4. If intravascular access devices are potentially the source of severe sepsis or septic shock, they should be promptly removed after establishing other vascular access.

Grade of Recommendation: E

#### E. Fluid Therapy

See initial resuscitation recommendations (A1–2) for timing of resuscitation.

1. Fluid resuscitation may consist of natural or artificial colloids or crystalloids. There is no evidence-based support for one type of fluid over another.

Grade of Recommendation: C

2. Fluid challenge in patients with suspected hypovolemia (suspected inadequate arterial circulation) may be given at a rate of 500–1,000 mL of crystalloids or 300–500 mL of colloids over 30 mins and repeated based on response (increase in blood pressure and urine output) and tolerance (evidence of intravascular volume overload).

Grade of Recommendation: E

#### F. Vasopressors

1. When an appropriate fluid challenge fails to restore adequate blood pressure and organ perfusion, therapy with vasopressor agents should be started. Vasopressor therapy may also be required transiently to sustain life and maintain perfusion in the face of life-threatening hypotension, even when a fluid challenge is in progress and hypovolemia has not yet been corrected.

Grade of Recommendation: E

2. Either norepinephrine or dopamine (through a central catheter as soon as available) is the first-choice vasopressor agent to correct hypotension in septic shock

Grade of Recommendation: D

3. Low-dose dopamine should not be used for renal protection as part of the treatment of severe sepsis.

Grade of Recommendation: B

4. All patients requiring vasopressors should have an arterial catheter placed as soon as practical if resources are available.

Grade of Recommendation: E

5. Vasopressin use may be considered in patients with refractory shock despite adequate fluid resuscitation and high-dose conventional vasopressors. Pending the outcome of ongoing trials, it is not recommended as a replacement for norepinephrine or dopamine as a first-line agent. If used in adults, it should be administered at infusion rates of 0.01– 0.04 units/min. It may decrease stroke volume.

Grade of Recommendation: E

#### G. Inotropic Therapy

1. In patients with low cardiac output despite adequate fluid resuscitation, dobutamine may be used to increase cardiac output. If used in the presence of low blood pressure, it should be combined with vasopressor therapy.

Grade of Recommendation: E



2. A strategy of increasing cardiac index to achieve an arbitrarily predefined elevated level is not recommended.

Grade of Recommendation: A

#### H. Steroids

1. Intravenous corticosteroids (hydrocortisone 200–300 mg/day, for 7 days in three or four divided doses or by continuous infusion) are recommended in patients with septic shock who, despite adequate fluid replacement, require vasopressor therapy to maintain adequate blood pressure.

Grade of Recommendation: C

- a. Some experts would use a 250-microgram adrenocorticotrophic hormone (ACTH) stimulation test to identify responders (>9 micrograms/dL increase in cortisol 30–60 mins post-ACTH administration) and discontinue therapy in these patients. Clinicians should not wait for ACTH stimulation results to administer corticosteroids.

Grade of Recommendation: E

- b. Some experts would decrease dosage of steroids after resolution of septic shock.

Grade of Recommendation: E

- c. Some experts would consider tapering the dose of corticosteroids at the end of therapy.

Grade of Recommendation: E

- d. Some experts would add fludrocortisone (50 micrograms orally four times per day) to this regimen.

Grade of Recommendation: E

2. Doses of corticosteroids >300 mg hydrocortisone daily should not be used in severe sepsis or septic shock for the purpose of treating septic shock.

Grade of Recommendation: A

3. In the absence of shock, corticosteroids should not be administered for the treatment of sepsis. There is, however, no contraindication to continuing maintenance steroid therapy or to using stress dose steroids if the patient's history of corticosteroid administration or the patient's endocrine history warrants.

Grade of Recommendation: E

I. Recombinant Human Activated Protein C (rhAPC)

1. rhAPC is recommended in patients at high risk of death (Acute Physiology and Chronic Health Evaluation II  $\geq 25$ , sepsis-induced multiple organ failure, septic shock, or sepsis-induced acute respiratory distress syndrome [ARDS]) and with no absolute contraindication related to bleeding risk or relative contraindication that outweighs the potential benefit of rhAPC. (See Appendix B in original guideline document for absolute contraindications and prescription information for warnings.)

Grade of Recommendation: B

J. Blood Product Administration

1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as significant coronary artery disease, acute hemorrhage, or lactic acidosis (see recommendations for initial resuscitation), red blood cell transfusion should occur only when hemoglobin decreases to  $< 7.0$  g/dL ( $< 70$  g/L) to target a hemoglobin of 7.0–9.0 g/dL.

Grade of Recommendation: B

2. Erythropoietin is not recommended as a specific treatment of anemia associated with severe sepsis but may be used when septic patients have other accepted reasons for administration of erythropoietin such as renal failure induced compromise of red blood cell production.

Grade of Recommendation: B

3. Routine use of fresh frozen plasma to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures is not recommended.

Grade of Recommendation: E

4. Antithrombin administration is not recommended for the treatment of severe sepsis and septic shock.

Grade of Recommendation: B

5. In patients with severe sepsis, platelets should be administered when counts are  $< 5,000/\text{mm}^3$  ( $5 \times 10^9/\text{L}$ ) regardless of apparent bleeding. Platelet transfusion may be considered when counts are 5,000–30,000/ $\text{mm}^3$  ( $5\text{--}30 \times 10^9/\text{L}$ ) and there is a significant risk of bleeding. Higher platelet counts ( $\geq 50,000/\text{mm}^3$  [ $50 \times 10^9/\text{L}$ ]) are typically required for surgery or invasive procedures.

Grade of Recommendation: E

K. Mechanical Ventilation of Sepsis-Induced Acute Lung Injury (ALI)/ARDS

1. High tidal volumes that are coupled with high plateau pressures should be avoided in ALI/ARDS. Clinicians should use as a starting point a reduction in tidal volumes over 1–2 hrs to a "low" tidal volume (6 mL per kilogram of predicted body weight) as a goal in conjunction with the goal of maintaining end-inspiratory plateau pressures <30 cm H<sub>2</sub>O. (See Appendix C in the original guideline document for a formula to calculate predicted body weight.)

Grade of Recommendation: B

2. Hypercapnia (allowing PaCO<sub>2</sub> to increase above normal, so-called permissive hypercapnia) can be tolerated in patients with ALI/ARDS if required to minimize plateau pressures and tidal volumes.

Grade of Recommendation: C

3. A minimum amount of positive end-expiratory pressure should be set to prevent lung collapse at end-expiration. Setting positive end-expiratory pressure based on severity of oxygenation deficit and guided by the FIO<sub>2</sub> required to maintain adequate oxygenation is one acceptable approach. (See Appendix C in the original guideline document.) Some experts titrate positive end-expiratory pressure according to bedside measurements of thoracopulmonary compliance (to obtain the highest compliance, reflecting lung recruitment).

Grade of Recommendation: E

4. In facilities with experience, prone positioning should be considered in ARDS patients requiring potentially injurious levels of FIO<sub>2</sub> or plateau pressure who are not at high risk for adverse consequences of positional changes.

Grade of Recommendation: E

5. Unless contraindicated, mechanically ventilated patients should be maintained semirecumbent, with the head of the bed raised to 45 degrees to prevent the development of ventilator-associated pneumonia.

Grade of Recommendation: C

6. A weaning protocol should be in place and mechanically ventilated patients should undergo a spontaneous breathing trial to evaluate the ability to discontinue mechanical ventilation when they satisfy the following criteria: a) arousable; b) hemodynamically stable (without vasopressor agents); c) no new potentially serious conditions; d) low ventilatory and end-expiratory pressure requirements; and e) requiring levels of FIO<sub>2</sub> that could be safely delivered with a face mask or nasal cannula. If the spontaneous breathing trial is successful, consideration should be given for extubation (see Appendix D of the original guideline document). Spontaneous breathing trial options

include a low level of pressure support with continuous positive airway pressure 5 cm H<sub>2</sub>O or a T-piece.

Grade of Recommendation: A

L. Sedation, Analgesia, and Neuromuscular Blockade in Sepsis

1. Protocols should be used when sedation of critically ill mechanically ventilated patients is required. The protocol should include the use of a sedation goal, measured by a standardized subjective sedation scale.

Grade of Recommendation: B

2. Either intermittent bolus sedation or continuous infusion sedation to predetermined end points (e.g., sedation scales) with daily interruption/lightening of continuous infusion sedation with awakening and retitration, if necessary, are recommended methods for sedation administration.

Grade of Recommendation: B

3. Neuromuscular blockers should be avoided if at all possible in the septic patient due to the risk of prolonged neuromuscular blockade following discontinuation. If neuromuscular blockers must be used for longer than the first hours of mechanical ventilation, either intermittent bolus as required or continuous infusion with monitoring of depth of block with train of four monitoring should be used.

Grade of Recommendation: E

M. Glucose Control

1. Following initial stabilization of patients with severe sepsis, maintain blood glucose <150 mg/dL (8.3 mmol/L). Studies supporting the role of glycemic control have used continuous infusion of insulin and glucose. With this protocol, glucose should be monitored frequently after initiation of the protocol (every 30– 60 mins) and on a regular basis (every 4 hrs) once the blood glucose concentration has stabilized.

Grade of Recommendation: D

2. In patients with severe sepsis, a strategy of glycemic control should include a nutrition protocol with the preferential use of the enteral route.

Grade of Recommendation: E

N. Renal Replacement

1. In acute renal failure, and in the absence of hemodynamic instability, continuous venovenous hemofiltration and intermittent hemodialysis are considered equivalent. Continuous hemofiltration offers easier

management of fluid balance in hemodynamically unstable septic patients.

Grade of Recommendation: B

O. Bicarbonate Therapy

1. Bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements is not recommended for treatment of hypoperfusion-induced lactic acidemia with pH  $\geq 7.15$ . The effect of bicarbonate administration on hemodynamics and vasopressor requirement at lower pH, as well as the effect on clinical outcome at any pH, has not been studied.

Grade of Recommendation: C

P. Deep Vein Thrombosis Prophylaxis

1. Severe sepsis patients should receive deep vein thrombosis (DVT) prophylaxis with either low-dose unfractionated heparin or low-molecular weight heparin. For septic patients who have a contraindication for heparin use (i.e., thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral hemorrhage), the use of a mechanical prophylactic device (graduated compression stockings or intermittent compression device) is recommended (unless contraindicated by the presence of peripheral vascular disease). In very high-risk patients such as those who have severe sepsis and history of deep vein thrombosis, a combination of pharmacologic and mechanical therapy is recommended.

Grade of Recommendation: A

Q. Stress Ulcer Prophylaxis

1. Stress ulcer prophylaxis should be given to all patients with severe sepsis. H<sub>2</sub> receptor inhibitors are more efficacious than sucralfate and are the preferred agents. Proton pump inhibitors have not been assessed in a direct comparison with H<sub>2</sub> receptor antagonists and, therefore, their relative efficacy is unknown. They do demonstrate equivalency in ability to increase gastric pH.

Grade of Recommendation: A

R. Consideration for Limitation of Support

1. Advance care planning, including the communication of likely outcomes and realistic goals of treatment, should be discussed with patients and families. Decisions for less aggressive support or withdrawal of support may be in the patient's best interest.

Grade of Recommendation: E

S. Pediatric Considerations

Refer to the original guideline document for pediatric considerations in the following areas:

1. Mechanical Ventilation
2. Fluid Resuscitation
3. Vasopressors/Inotropes (should only be used after appropriate volume resuscitation)
4. Therapeutic End Points
5. Approach to Pediatric Septic Shock
6. Steroids
7. Protein C and Activated Protein C
8. Granulocyte Macrophage Colony Stimulating Factor
9. Deep Vein Thrombosis Prophylaxis
10. Stress Ulcer Prophylaxis
11. Renal Replacement Therapy
12. Glycemic Control
13. Sedation/Analgesia
14. Blood Products
15. Intravenous Immunoglobulin
16. Extracorporeal membrane oxygenation (ECMO)

#### Definitions:

#### Grades of Evidence

- I. Large, randomized trials with clear-cut results; low risk of false-positive (alpha) error of false-negative (beta) error
- II. Small, randomized trials with uncertain results; moderate-to-high risk or false-positive (alpha) and/or false-negative (beta) error
- III. Nonrandomized, contemporaneous controls
- IV. Nonrandomized, historical controls and expert opinion
- V. Case series, uncontrolled studies, and expert opinion

#### Grades of Recommendation

- A. Supported by at least two level I investigations
- B. Supported by one level I investigation
- C. Supported by level II investigations only
- D. Supported by at least one level III investigation
- E. Supported by level IV or V evidence

#### CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for the Resuscitation of Pediatric Septic Shock.

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Improved management and outcomes of patients with severe sepsis and septic shock in intensive care unit and pre-intensive care unit settings

### POTENTIAL HARMS

Side effects of medication, for example:

- Recombinant human activated protein C (rhAPC) increases the risk of bleeding.
- Dopamine causes more tachycardia and may be more arrhythmogenic than norepinephrine.
- Vasopressin therapy may result in decreased cardiac output and hepatosplanchnic flow.

Complications of treatments, for example:

- Arterial catheter placement may result in hemorrhage and damage to arterial vessels.
- Source control interventions may cause further complications such as bleeding, fistulas, or inadvertent organ injury.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

#### Recombinant Human Activated Protein C (rhAPC)

rhAPC is contraindicated in patients with the following clinical situations in which bleeding could be associated with a high risk of death or significant morbidity:

- active internal bleeding
- recent (within 3 months) hemorrhagic stroke
- recent (within 2 months) intracranial or intraspinal surgery or severe head trauma
- trauma with an increased risk of life-threatening bleeding
- presence of an epidural catheter
- intracranial neoplasm or mass lesion or evidence of cerebral herniation

#### Heparin

Contraindications to heparin use include thrombocytopenia, severe coagulopathy, active bleeding, and recent intracerebral hemorrhage.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

These recommendations are intended to provide guidance for the clinician caring for a patient with severe sepsis or septic shock, but they are not applicable for all patients. Recommendations from these guidelines cannot replace the clinician's decision-making capability when he or she is provided with a patient's unique set of clinical variables. Although these recommendations are written primarily for the patient in the intensive care unit (ICU) setting, many recommendations are appropriate targets for the pre-ICU setting. It should also be noted that resource limitations may prevent physicians from accomplishing a recommendation.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better

### IOM DOMAIN

Effectiveness  
Timeliness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, Ramsay G, Zimmerman JL, Vincent JL, Levy MM. Surviving sepsis campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004 Mar;32(3):858-73. [135 references] [PubMed](#)

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2004 Mar



## GUIDELINE DEVELOPER(S)

Society of Critical Care Medicine - Professional Association

## SOURCE(S) OF FUNDING

Society of Critical Care Medicine (SCCM)

## GUIDELINE COMMITTEE

Surviving Sepsis Campaign Management Guidelines Committee

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Meeting expenses as well as staff support for guidelines creation were provided by unrestricted industry educational grants as listed in the original guideline document. There were no industry members of the committee. There was no industry input into guidelines development and no industry presence at any of the meetings. Industry awareness or comment on the recommendations was not allowed. The sponsors of the educational grants did not see the recommendations until the manuscript was peer reviewed and accepted for publication in final form.

Each participant completed a conflict of interest form, and individuals were not assigned to a subgroup topic if they had a potential conflict of interest.

### Faculty Disclosures—Potential Conflicts of Interest

Speakers bureau, consultant fees, or research grants; Richard J. Beale, MD (Eli Lilly, Fresenius Hemocare and Fresenius Kabi); E. David Bennett, MD (Deltex, Ltd.); Pierre-Yves Bochud, MD (Swiss National Science Foundation); Christian Brun-Buisson, MD (Arrow Int'l, Eli Lilly, Glaxo-Smith-Kline, Roche, Wyeth-Lederle); Thierry Calandra, MD (Pfizer, Merck, NatImmune); Jean M. Carlet, MD (Eli Lilly, Anbics, Novo Nordisk, Wyeth Lederle, Fujisawa, Glaxo-Smith-Kline, Bayer, Abbott, Intrabiotics); Jonathan Cohen, MD (Glaxo-Smith-Kline); Catherine

Cordonnier, MD (Gilead Science, Merck, Pfizer, Fujisawa); E. Patchen Dellinger, MD (Glaxo-Smith-Kline, Bayer, Eli Lilly, Merck, Wyeth-Ayerst, Pfizer, Ortho-McNeil, Chiron, Versicor, InterMune, Peninsula); R. Phillip Dellinger, MD (Aventis, Bayer, Cubist, Edwards, Eli Lilly, Ortho Biotech, Wyeth-Ayerst); Roger G. Finch, MD (Cubist, Bayer, Glaxo-Smith-Kline, AstraZeneca, Bristol Myers Squibb, Aventis); Francois A. Fourrier, MD (Laboratoire Francais du fractionnement et des biotechnologies [LFB]); Jan A. Hazelzet, MD (Baxter, Eli Lilly); James H. Jorgensen, PhD (bio-Merieux Inc., Becton-Dickinson); Didier Keh, MD (Deutsche Forschungsgemeinschaft [DFG]); Mitchell M. Levy, MD (Eli Lilly, Edwards Lifesciences, OrthoBiotech); Dennis G. Maki, MD (Eli Lilly, Becton Dickinson, Johnson and Johnson); John C. Marshall, MD (Glaxo-Smith-Kline, Eli Lilly, Wyeth-Ayerst, Eisai, Centocor, Boehringer-Ingelheim); Henry Masur, MD (Cubist); Glenn S. Murphy, MD (Organon, Inc.); Steven M. Opal, MD (Genetics Institute, Chiron, Eli Lilly); Margaret M. Parker, MD (Johnson & Johnson [Ortho Bio-tech] – member of Independent Data Monitoring Committee for epo trial); Joseph E. Parrillo, MD (Eisai American, Inc., Schering-Plough Co., Glaxo-Smith-Kline, Medinox, Inc., Chiron Corp., Edwards Lifesciences, Ortho Biotech); Andrew Rhodes, MD (Edwards Lifesciences); Charles L. Sprung, MD, JD (AstraZeneca, European Commission, Eli Lilly); Antoni Torres, MD (Aventis, Abbott, Bayer); Stephen Trzeciak, MD (Aventis, Eli Lilly, Edwards Lifesciences); Jeffery S. Vender, MD (Abbott Pharmaceuticals); Jean-Louis Vincent, MD, PhD (Baxter, Brahms, BMS, Eli Lilly, Glaxo-Smith-Kline, Edwards, Pfizer); Janice L. Zimmerman, MD (Glaxo-Smith-Kline, Cubist)

Direct financial interest – stock (\$10,000 or more) or partial ownership; None. Faculty with no relationship to disclose; Marc Bonten, MD; Joseph A. Carcillo, MD; Alain Cariou, MD; Jean-Francois Dhainaut, MD, PhD; Simon Finfer, MD; Juan Gea-Banacloche, MD; Herwig Gerlach, MD, PhD; Maurene A. Harvey, RN, MPH; Steven M. Hollenberg, MD; Ronald V. Maier, MD; John J. Marini, MD; Martin Nitsun, MD; Graham Ramsay, MD; Jonathan E. Sevransky, MD; Joseph W. Szokol, MD; Christophe Vinsonneau, MD

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## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Dorman T, Angood PB, Angus DC, Clemmer TP, Cohen NH, Durbin CG Jr, Falk JL, Helfaer MA, Haupt MT, Horst HM, Ivy ME, Ognibene FP, Sladen RN,

Grenvik AN, Napolitano LM. Guidelines for critical care medicine training and continuing medical education. Crit Care Med 2004 Jan; 32(1):263-72.

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#### PATIENT RESOURCES

None available

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Date Modified: 11/8/2004

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